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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/791,296 | 03/03/2004 | Barbara S. Slusher | 054707-1262 | 3545 |

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| EXAMINER | |
|---|---|
| OLSON, ERIC | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/791,296 | SLUSHER ET AL. | |
| | Examiner | Art Unit | |
| | Eric S. Olson | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Detailed Action**

This application claims benefit of provisional application 60/450690, filed March 3, 2003. Claims 1-47 are pending in this application and subject to restriction and election of species herein.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 3-7, drawn to a method for treating opioid tolerance comprising administering a compound of formula (I) to a mammal, and pharmaceutical compositions for use in said method, classified in class 514, subclass 557 or 561, for example.

II. Claims 8-12 and 43-45, drawn to a method for treating opioid tolerance comprising administering a compound of formula (I) or (XV) to a mammal and pharmaceutical compositions for use in said method, classified in class 514, subclass 557 or 561, for example.

III. Claims 31, 32, and 36-38 in part and 13-18, 25-30, 33, 34, 39, 40, and 42 in full, drawn to a method for treating opioid tolerance comprising administering an aryl carboxylate compound of any of formula (VI), (VII), or (IX)-(XIV) to a mammal and pharmaceutical compositions for use in said method, classified in class 514, subclass 568 or 569, for example.

IV. Claims 31, 32, and 36-38 in part and 19-24, 35, and 41 in full drawn to a method for treating opioid tolerance comprising administering an aliphatic acid substituted with a benzene ring, of any of formula (VIII), (IX), (XIII), or

(XIV) to a mammal and pharmaceutical compositions for use in said method, classified in class 514, subclass 570 or 571, for example.

Claims 1-2 and 47 link inventions I-IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims. Upon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claims will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01

The inventions are distinct, each from the other because of the following reasons:

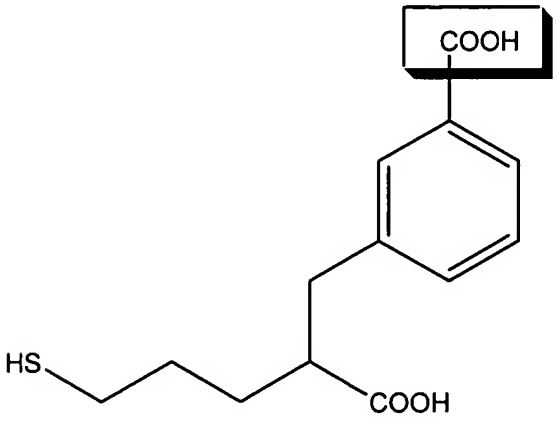
Inventions I and II are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the therapeutic agents used in the inventions are structurally distinct from one another. Chemical structures which are similar are presumed to function similarly, while chemical structures which are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of ***Application of Papesch, 50 CCPA 1084, 315 F.2s 381, 137 USPQ 43 (CCPA 1963)***, and ***In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984)***, chemical structures are patentably distinct where structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure. In the instant case, the structures differ in that the compounds of formula I contain a phosphonate or phosphinate while those of formula II contain an amide, ketone, thioketone, ketal, or similar carbonyl group. These two functional groups differ in their electrostatic and hydrogen bonding properties, and thus in their ability to interact with and inhibit various proteins. This is particularly relevant because these compounds are intended for use as NAALADase

inhibitors. Because NAALADase is a peptidase, it is expected to be particularly sensitive to the presence of amides, esters, thioesters, and the like.

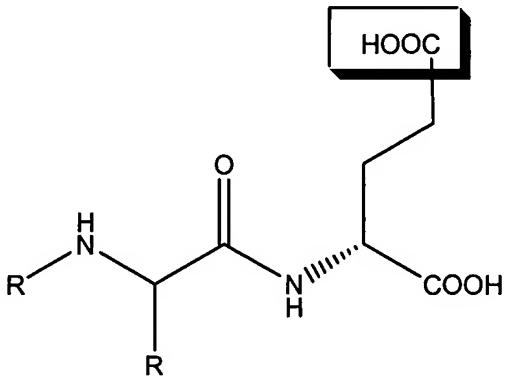
Because these inventions are distinct for the reasons given above and the search required for group I is not required for group II, restriction for examination purposes as indicated is proper.

Inventions III and IV are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the therapeutic agents used in the inventions are structurally distinct from one another. Chemical structures which are similar are presumed to function similarly, while chemical structures which are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of ***Application of Papesch, 50 CCPA 1084, 315 F.2s 381, 137 USPQ 43 (CCPA 1963)***, and ***In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984)***, chemical structures are patentably distinct where structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure. In the instant case, the structures

differ in that the compounds of group III contain an aromatic carboxylate group while the compounds of group IV contain only aliphatic acid groups. This is particularly significant because of the structures of the claimed NAALADase inhibitors compared to the natural substrate of NAALADase, as shown below:




NAALADase Inhibitor



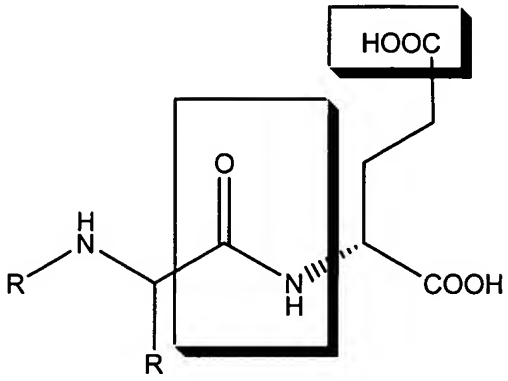

NAALADase natural substrate

Since NAALADase is specific for carboxy-terminal glutamate residues, the presence (in group III) or absence (in group IV) of the highlighted carboxylate residue is expected to lead to a significant difference in the interactions between the inhibitors and their target.

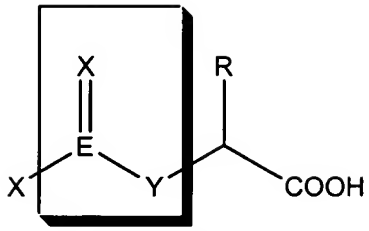
Because these inventions are distinct for the reasons given above and the search required for group III is not required for group IV, restriction for examination purposes as indicated is proper.

Inventions I and II are directed to related processes to inventions III and IV. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the

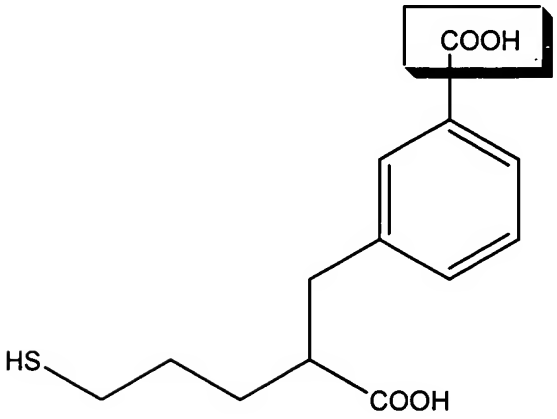
inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the therapeutic agents used in the inventions are structurally distinct from one another. Chemical structures which are similar are presumed to function similarly, while chemical structures which are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of ***Application of Papesch, 50 CCPA 1084, 315 F.2s 381, 137 USPQ 43 (CCPA 1963)***, and ***In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984)***, chemical structures are patentably distinct where structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure. In the instant case, the inhibitors of groups I-II represent a fundamentally different design from those of groups III-IV. Groups I-II. The structures of the different inhibitors are shown below:



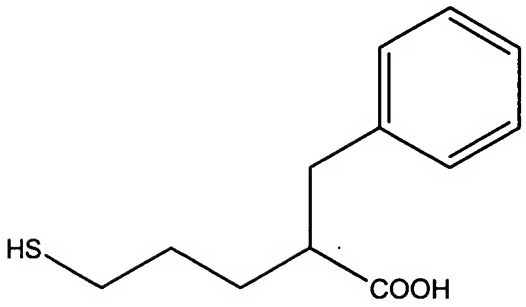

NAALADase natural substrate




Groups I-II




Group III




Group IV

The inhibitors of groups I-II mimic the natural substrate by incorporating an electrophilic group which mimics the peptide bond of the natural substrate. The inhibitors of groups III-IV do not include this electrophile, and the inhibitors of group III additionally include a carboxylate group to mimic the glutamate side chain. Because of the differing design of the various inhibitors, they are expected to interact differently with their targets and to exert different biological effects. The therapeutic methods utilizing them are thus patentably distinct.

Because these inventions are distinct for the reasons given above and the search required for groups I and II is not required for groups III and IV, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species: a plurality of various NAALADase inhibitors to be used as therapeutic agents in the claimed methods. The species are independent or distinct because they possess distinct chemical structures.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-3, 8, 16, 19, 22, 25, 27, 29, 31, 37, and 43 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103(a) of the other invention.

Because the above restriction requirement is complex, a telephone call to applicant's agent to request an oral election was not made. (See MPEP 812.01) Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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